Update: Availability of Varicella Zoster Immune Globulin

Advisory Committee for Blood Safety and Availability

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Dorothy Scott, M.D.

OBRR/CBER

Varicella Zoster Immune Globulin (VZIG)

- Licensed in 1981
- Intramuscular preparation sourced from selected high anti-VZV plasma units
- Indications – Prevention/Modification of severe varicella disease (pneumonia, hepatitis, encephalitis, mortality) in:
  - Immune compromised children and adults
  - Premature infants
  - Infants < 1 year age
  - Selected non-immune pregnant women and healthy adults
- Should be administered within 96 hours of varicella exposure

VZIG Supply

- Sole manufacturer – Massachusetts Public Health Biological Laboratories (MPHBL)
- MPHBL plasma fractionation facility scheduled to close
- VZIG Supply – anticipated to last until 1/2006
- Vials/year used ~ 10,000 125 U vials (depending on weight, 2,000 – 10,000 patients)
- FDA Actions –
  - Encourage new IND's for VZIG
  - Define paths to licensure: BPAC meeting 7/21/05
  - Supply monitoring
  - Communication with CDC
  - Public communication

Questions to the Committee

1. Please discuss what laboratory and clinical data would be sufficient to demonstrate efficacy of a new anti-varicella antibody preparation, for prophylaxis of severe varicella infection. In particular, please comment on
   a. Which target populations would be most informative to study
   b. What surrogate markers would be appropriate for assessment of efficacy
   c. Other considerations for clinical trials
2. Please comment on whether the available scientific data support use of IGIV or acyclovir as a substitute for VZIG for prophylaxis of severe VZV infection in any clinical settings

BPAC 7/21/05 Questions

- Target populations
  - Low numbers of susceptible people due to vaccination
  - Difficult to study in a short time-frame due to variety of clinical situations but small numbers of subjects
- Surrogate markers
  - PK equivalence in normal subjects compared to licensed VZIG; laboratory demonstrations of equivalence compared to licensed product
  - Phase 4 commitment to further study
- Could IGIV substitute?
  - Uncertain, because lot-lot titers not known
  - Titers may diminish as vaccinated donors replace naturally infected donors
- Could acyclovir substitute?
  - No, because efficacy evidence not sufficient

Speakers

1. Donna Ambrosino, M.D., and Catherine Hay, Ph.D., MPHBL. VZIG manufacture, potency testing, and current supply status.
2. Philip LaRussa, M.D., Professor of Clinical Pediatrics, Columbia University. Severe Varicella Zoster disease, correlates of protection, and post-exposure prophylaxis options.
3. Mona Marin, M.D., NIP/CDC. ACIP and Red Book recommendations for post-exposure prophylaxis of severe varicella zoster infections

Current Situation

- Ongoing supply monitoring – FDA, in communication with FFF Enterprises (distributor) and MPHBL
- Requests only on an as-needed basis from FFF encouraged
- Review of INDs
  - Eligible to request orphan drug classification
  - Eligible to request cost recovery for IND product
  - Treatment protocols will be considered
- Communication – website posting
  - Licensed uses
  - How to obtain VZIG

VZIG Usage

- Clinicians and pharmacies encouraged to order only for identified patients in need of VZIG, rather than for inventory
- VZIG can be ordered from FFF Enterprises at 1-800-843-7477
- Can be delivered within 24 hours of request under normal circumstances
- Potential for hospital-hospital transfer of VZIG inventory if needed

VZIG Pivotal Trial for Licensure[1]

	VZIG	ZIG	Historical controls[2]
Pox count > 100	12/81 (15%)	13/83 (16%)	87%
Pneumonia	3/81 (4%)	3/83 (4%)	25%
Hepatitis	0	0	10%
Encephalitis	0	0	5%
Death	0	0	7%

[1] Zaia et al, JID 147: 737-43, 1983.

[2] Feldman et al, Pediatrics 56:388-97, 1975